

# Notice of Allowability

Application No.

09/853,033

Examiner

Celine X. Qian Ph.D.

Applicant(s)

CHAMBON ET AL.

Art Unit

1636

## -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to to the amendment filed on 1/20/06.
2. ☒ The allowed claim(s) is/are 69, 74-86.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
  1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

## Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

### EXAMINER'S AMENDMENT

An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. During a telephone conversation conducted on 2/21/06, Applicant's representative requested an extension of time for one MONTH(S) and authorized the Director to charge Deposit Account No. 19-0741 for this extension and authorized the following examiner's amendment. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

The application has been amended as follows:

Claim 69. A method for producing spatio-temporally-controlled site-specific somatic recombinations in a mouse, wherein one or more gene or intergenic DNA sequences of interest naturally belonging to the genome of said mouse have been recombined, comprising:

a) obtaining a transgenic mouse, wherein said transgenic mouse comprises a transgene encoding:

(i) a Cre fusion protein comprising sequentially:

(1) a Cre recombinase protein;

a hinge region of at least 15 amino acids ;

a polypeptide comprising the ligand binding domain of the human nuclear estrogen receptor, or of a vertebrate nuclear estrogen receptor, said polypeptide exhibiting at least one mutation relative to the wild-type form of said ligand binding domains; and

(2) has a negligible, or even zero recombinase activity in the absence of a synthetic ligand endowed with antiestrogenic activity, the recombinase activity being induced by low dose of the synthetic ligand;

[(i)] (ii) one or more gene or intergenic DNA sequences of interest, naturally belonging to the mouse genome, flanked by one or more recognition sites for a Cre recombinase protein, [and are located in one or more of the chromosomes of the genome of said mouse; and]

[(ii) a Cre fusion protein comprising sequentially:

(1) a Cre recombinase protein;

a hinge region of at least 15 amino acids ;

a polypeptide comprising the ligand binding domain of the human nuclear estrogen receptor, or of a vertebrate nuclear estrogen receptor, said polypeptide exhibiting at least one mutation relative to the wild-type form of said ligand binding domains; and

(2) has a negligible, or even zero recombinase activity in the absence of a synthetic ligand endowed with antiestrogenic activity, the recombinase activity being induced by low dose of the synthetic ligand; ]

b) administering to said transgenic mouse a low dose of said synthetic ligand in order to induce Cre-mediated recombination; and

c) said gene or intergenic DNA sequences of interest undergo a site specific somatic recombination, as a result of the induction by said synthetic ligand, in at least 90% of the targeted cells of said mouse, whereas said gene or intergenic sequences of interest underwent

Art Unit: 1636

recombination in less than 5% of the targeted cells of said mouse before step b). [obtaining a recombined mouse, wherein said recombined mouse has undergone a site-specific somatic recombination of said gene or intergenic DNA sequences as a result of the induction, by said synthetic ligand, of specific recombination aid gene or intergenic DNA sequences by said Cre fusion protein in at least 90% of the targeted cells of said mouse, whereas less than 5% of the targeted cells of said mouse underwent recombination of said gene or intergenic DNA sequences before step b).]

Claim 78. The method of claim 69, wherein said [Cre fusion protein is encoded by a fusion gene integrated into one or more of the chromosomes of said cell of said mouse, said fusion gene] transgene is [being] under the control of expression elements ensuring its expression in the targeted cells of said mouse.

Claim 82. The method of claim 78, wherein said [fusion gene] transgene has [having] the sequence SEQ ID NO:5, which encodes the fusion protein Cre-ER<sup>T2</sup> having the sequence SEQ ID NO:6.

Claim 83. The method of claim 69, wherein said DNA sequence of interest comprises the RXR $\alpha$  gene [is a gene comprising RXR $\alpha$ ].

Claim 84. The method of 69, wherein the genome of said mouse comprises:

-a transgene [fusion gene] encoding the fusion Cre-ER<sup>T2</sup> having the sequence SEQ ID NO:6, said fusion protein [gene] being selectively expressed in adipocytes under the control of the adipocyte fatty acid binding protein 2 (aP2) promoter; and

-one or more chromosomal DNA sequence of interest in their natural chromatin context and flanked on each sided by one lox site, the two lox sites being oriented as a direct repeat.

Art Unit: 1636

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.  
Examiner  
Art Unit 1636

CELINE QIAN, PH.D.  
PRIMARY EXAMINER

